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BIOARTIFICIAL LIVER- A REVIEW

Deepa. M[1], Ravindra Reddy. K [2] Bhuvaneswari. S[1], Arshiya Banu.S [1], Madhu Bindu.A[1], Siri mamatha.C[1]

[1]P. Rami Reddy Memorial College of Pharmacy, Kadapa, A.P – 516003, India

[2]C.E.S College of pharmacy, Kurnool, Andhra Pradesh, India

ABSTRACT

Bioartifical livers are potentially effective countermeasures against liver failure. Bioartifical liver support devices were developed, which requires separation methods between the patient's blood and the liver support bioreactors that guarantee the sufficient transfer of pathophysiologically relevant substances but prevent complications. Without bioartificial liver transplantation, liver failure has been associated with high morbidity and mortality. This review focuses on the brief overview and development of bioartificial liver system which acts as a bridge for the patients who are suffering from the acute liver failure until a transplant is done or to give the recipient's liver time to recover its function. It has proven that treatments with bioartificial devices are indeed safe.

Key words: Acute liver failure, Bioartificial livers**,** Bioreactors, hepatocytes.

INTRODUCTION:

Liver is a one of the chief organ in our body with various vital functions in synthesis, detoxification and regulation. Not only this but it also used to fight with infections, helps to digest food and stores energy for when you need it and clean your blood. Such a organ failure therefore constitutes a life threatening condition. For the severe liver failure patients, liver transplantation was the only available treatment but there aren't enough donors to fill the need. People needing a liver transplant was placed on a national waiting list for organ Sharing. In order to minimise this risk, Bioartificial liver system was introduced. It has become a promising treatment modality for liver failure. It shows a huge success as a temporary support for potential transplant recipients as well as for the patients with reversible acute hepatitis who do not qualify for liver transplantation.

Address for correspondence

Deepa. M*
P. Rami Reddy Memorial College of Pharmacy,
Kadapa, A.P – 516003, India
E-mail: venkatdeepa19@gmail.com

This device employing isolated liver cells or hepatocytes can potentially provide temporary support for the patients suffering from acute liver failure.

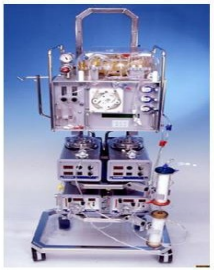
HISTORY:

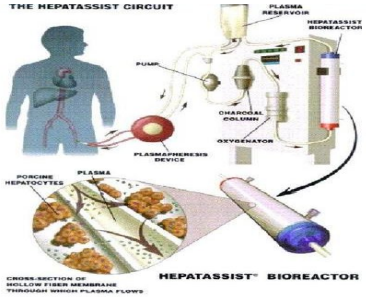
Despite recent advances in medical therapy, patients with fulminant hepatic failure (FHF) have a mortality rate approaching 90%[1]. Because of failure to arrest the progression of cerebral oedema, many patients die. Liver transplantation has improved survival to 65% to 75%. However, there is a shortage of donors and approximately one half of the patients with FHF will die while waiting for liver transplantation. There is thus a need to develop a system which helps to keep these patients alive and neurologically intact until either an organ becomes available for transplantation or the native liver recovers from injury. According to the statistics gathered by World Health Organisation(WHO), hepatitis causes more than a million deaths a year and many of those who survive from hepatitis develop cirrhosis and chronic liver failure. Because of this intensive research was carried out & efforts have been made to optimize the allocation of organs for the treatment of fulminant liver failure. For years, it seemed to develop an artificial liver which would

be impossible. A break through occurred when Dr. Kenneth Matsumara took a completely different approach, he designed a device that uses liver cells obtained from animals instead of trying for an artificial liver. This first bioartificial liver device developed by Dr. Kenneth Matsumara was named an invention of the year by Time magazine in 2001[2]. In this device, animal liver cells are suspended in a solution and a patient's blood are separated by a semi permeable that allow toxins and blood proteins to pass but restricts an immunological response[3]. There are both artificial and bioartificial livers for temporary support of liver. An artificial livers use non living component to remove the toxins accumulates during liver failure whereas Bio artificial livers have bioreactors containing hepatocytes to provide both biotransformation and synthetic liver functions. Because of this both aspects bioartifiial livers are considered as a effective temporary tool for the patients suffering from liver failure.

BIOARTIFICIAL LIVER:

Liver failure is the major cause of death for over 30,000 patients each year. To minimize this several extracorporeal bioartificial liver (BAL) devices are currently being evaluated as an alternative or adjunct therapy for liver disease. As this device contains both biological and manufactured components, it is called as "Bio-artificial liver". BAL devices show promise, in order to become a clinical reality and must clearly demonstrate efficacy in improving patient outcomes. These devices typically incorporate isolated cells into bioreactors to promote cell survival and function as well as provide for a level of transport seen *in vivo*. Bioartifical livers are essentially Bioreactors in which embedded hepatocytes perform the functions of a normal liver. Based on the design, the bioreactors are classified into four main types: hollow fiber, flat plate or monolayer cultures, perfused beds or scaffolds, and suspension or encapsulation chambers. Each design category has both pros and cons. Direct contact between plasma and the liver cells is guaranteed or those using semi-permeable membranes with high porosity are preferred in the bioreactors. In addition to this, liver cells need sufficient oxygen supply to function optimally[4] . The amount of oxygen actually dissolved in plasma is insufficient in this respect. Therefore, the cells in the bioreactor locally supply oxygen by oxygen capillaries interwoven with the cell containing hollow fibers (Modular Extracorporeal Liver Support)[5] or matrix (AMC-BAL)[6] inside the BAL and so called as internal oxygenator. Most common cellular component of BAL devices are primary porcine hepatocytes[7,8,9]. These are used in HepatAssit2000 system, Bioartificial Liver Support System(BLSS®) and LIVERX2000 System. Hepatocytes, liver cells, have a unique ability to reproduce after liver injury and consequently, the liver is capable of regeneration of lost tissue. These hepatocytes are kept in specially designed bioreactors which keep isolated liver cells in culture for long periods of time so that the cells are available for use in the liver assisting devices. Some other types of developing devices include the Extracorporal Liver Assisting Device (ELAD), Modular Extracorporeal Liver Support (MELS), and the Amsterdam Medical Center Bioartificial Liver (AMC-BAL). The Extracorporeal Liver Assist Device (ELAD)[10-15] (Houston, TX) is the only BAL device in which a human hepatocyte cell line (C3A) is used. But the high demand for donor organs makes it unlikely that sufficient excess tissue would be available for nontransplant applications. Furthermore, while mature hepatocytes proliferate rapidly *in vivo* during regeneration, primary human hepatocytes divide much less readily *in vitro* even under optimal culture conditions [16]. Several BAL devices are currently undergoing clinical testing for the treatment of liver disease and in each design, hollow fiber technology is used to separate cellular and perfusion compartments and to provide a basic scaffold for hepatocyte attachment. The most widely tested device, is HepatAssist. It is considering as important milestone that will provide valuable insight for future developments in the field. Because, HepatAssist treatment was associated with improvement in neurologic status[17,18].





According to Jul. 17, 2015 researchers have developed and are testing a device called the Spheroid Reservoir Bioartificial Liver (SRBAL) that can support healing and regeneration of the injured liver and improve outcomes and reduce mortality rates for patients suffering from acute liver failure without requiring a transplant. It improves survival in pigs. Although the bioartificial liver is not yet cleared in humans, these findings show promise as an effective treatment option for diseases like liver cancer and hepatitis which is becoming an increasingly common diagnosis. Future clinical studies are planned to assess the SRBAL as a less invasive, long-term treatment for liver transplantation [19].

FUNCTION AND USES OF BIOARTIFICIAL LIVER (BAL):

Bioartificial livers are vitally important bioreactors, embedded hepatocytes (liver cells) that perform the functions of a normal liver. Oxygenated blood plasma is separated from the other blood constituent[20] by this process. The purpose of BAL-type devices, currently, is not to permanently replace liver functions, but it serves as a supportive device either by allowing liver to regenerate properly on acute liver failure, or to bridge the individual's liver functions until a transplant is possible. BAL has both pros & cons. Some of the advantages are:

1. It monitors the state of liver cell functions during the treatment.
2. It improves survival for patients with fulminant and subfulminant liver failure.
3. It reduces mortality rate by 44% in acute liver failure patients.
4. Bridge the patient or Keep the patient alive until transplant is available
5. Aid in the livers regeneration

Bio-artificial livers should be able to provide at least 10% of liver functioning. It prevents manifestations of liver failure. A bioartificial liver and/or a liver assist device should be able to detoxify, regulate, and synthesize molecules in the fashion of a normal liver.

COMPARISON TO OTHER LIVER DIALYSIS:

Liver dialysis is a detoxification treatment for liver failure and looks similar to kidney dialysis. The advantages of using a BAL, over other dialysis-type devices (e.g. liver dialysis), is that the metabolic functions like lipid and plasma lipoprotein synthesis, regulation of carbohydrates, homeostasis, production of serum albumin and clotting factors, etc.), in addition to detoxification, can be replicated without the use of multiple devices. A series of studies in 2004 showed that a BAL device reduced mortality by about half in acute liver failure cases[22]. There are currently several BAL devices in clinical trials showing a promising effect. Many studies showed that BAL device reduced mortality rate about half in liver failure cases.

CONCLUSION:

The concept of BAL support has proven to be successful in both animal and human studies. A variety of extracorporeal devices for liver failure have been developed in the last decade which now offer management options in liver failure and was till recently widely available. In addition to this clinical application of BAL devices has proven safe. These device potentially may be used before a liver transplant, to support liver function until a liver transplant is available. Mostly, liver transplantation and blood purification therapy, including plasmapheresis, hemodiafiltration are the available treatments for patients with severe hepatic failure. But, after the invention of bioartifical liver system it became much more easier to save the lives of the patients suffering from fulminant and subfulminant hepatic failure. It shows an effective temporary liver support, which improves the chances of survival with or without a transplant being ultimately carried out. The main aim of this bioartificial liver device is to provide support to the liver while it recovers or regenerates and often as a method of stabilizing patients prior to liver transplantation. With the rapid progress of bioartificial livers it appears that it may play an effective role in the future management of liver failure too.

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